

Editorial

Is Erectile Dysfunction the “Tip of the Iceberg” of a Systemic Vascular Disorder?

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Erectile function is a psychoneurovascular phenomenon which ultimately culminates in an increase of arterial flow within the hypogastric-penile bed with the subsequent activation of the veno-occlusive mechanism of the corpora cavernosa [1]. Most cases of erectile dysfunction (ED) recognize a vascular etiology. Common risk factors for atherosclerosis have been frequently found in patients with ED. In addition, the extent of ED has been related to the number and severity of risk factors [2,3]. Moreover, abnormal sexual function has been reported in patients with vascular diseases such as myocardial infarction [4], cerebrovascular accidents [5], hypertension and peripheral arterial disease [2,6]. The link between ED and coronary artery disease (CAD) is further substantiated by a similar pathogenic involvement of NO pathway with an impairment of endothelium-dependent vasodilatation and late structural vascular abnormalities [6–8]. Thus, ED may be considered as the clinical manifestation of a disease affecting penile circulation as a part of a more generalized vascular disorder. The anecdotal report of O’Kane et al. [9] of 2 patients with ED who were recognized as having CAD after ED diagnosis raises the question whether or not and why ED may be considered a marker of ischemic heart disease.

1. ED as the “tip of the iceberg”

Atherosclerosis is a systemic disorder that uniformly affects all major vascular beds. Nevertheless, clinical manifestations of vascular diseases rarely appear

simultaneously in the same patient. This may occur because arteries supplying various districts (i.e. penis, heart, brain, lower limbs) do have different size. Fig. 1 depicts the hypothetical vascular situation of a patient with isolated ED. A >50% lumen obstruction (i.e. the cut-off to define a flow-limiting stenosis) of the penile artery is assumed to be present. It is known that the increase of arterial inflow within the corpora cavernosa needed to obtain a rigid erection is significant and minor abnormalities of this hemodynamic change are sufficient to cause ED [10]. At this early stage, the same plaque burden affecting penile circulation would be less likely to cause significant obstruction to blood flow in coronary, carotid or femoral arteries due to their larger artery size. When atherosclerosis process increases, coronary artery lumen becomes significantly reduced (>50% lumen obstruction) leading to specific symptoms (i.e. angina pectoris). At the same time, penile circulation would be even more obstructed. In the late phase of atherosclerosis, larger arteries become significantly involved so that signs of cerebral and peripheral ischaemia develop. If this explanation holds true, due to the small artery size supplying penile circulation, ED would represent an early clinical evidence of a diffuse, largely sub-clinical vascular disorder (“the tip of the iceberg”). If unrecognized in the early stage, ED would represent, late in the course of the process, just one of the many vascular syndromes caused by atherosclerosis.

Currently available data appear to support this explanation. There are few studies dealing with patients originally investigated for ED who were submitted to test for CAD. The prevalence of positive responses (exercise stress tests in most of the cases), averaged out at 20% (range between 5% and 56%) [11–15]. This suggests that, in early stage of atherosclerosis, tests used to search for concomitant CAD might be normal

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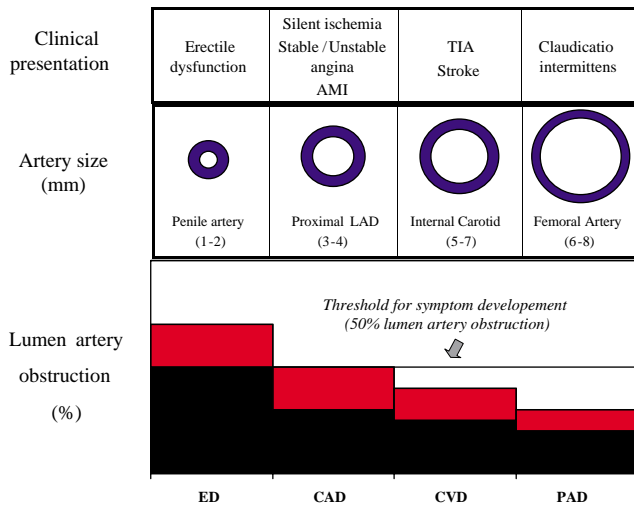


Fig. 1. Schematic drawing of atherosclerotic involvement of different vascular districts. The lower strip shows percent lumen artery obstruction. A >50% reduction in lumen artery size is the angiographic threshold required for symptom development. Black part of the figure represents plaque burden in a patient with isolated ED. Red part of the figure represents a later step of the atherosclerotic disease with greater plaque burden in a patient with clinically evident CAD. AMI: acute myocardial infarction, CAD: coronary artery disease, CVD: cerebrovascular disease, ED: erectile dysfunction, PAD: peripheral vascular disease, TIA: transient ischemic attack.

or unrevealing in about half to two-thirds of the patients likely because of non significant coronary artery involvement. As far as prevalence of silent carotid or femoral artery disease in patients with ED is concerned, there have been no population-based studies providing accurate data, although it would expected to be even lower than for CAD. When CAD becomes clinically evident, prevalence of ED has been reported to range between 44% and 65% [4,16–20], likely reflecting a concomitant, severe atherosclerotic involvement of penile circulation. We found a 49% prevalence of ED in a series of 300 consecutive patients with angiographically documented CAD. The intriguing finding was that in 67% of patients having both CAD and ED, the latter came well before anginal symptoms, with a mean time-interval of almost 3 years [21]. Finally, late in the vascular process, ED has been found to be as high as 86% and 87% in patients with symptomatic CVD and PAD, respectively [6,8,22–25].

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2. Exceptions to the rule

A wide range of ED prevalence in patients with various vascular diseases has been reported in the literature. Reasons are difference in population characteristics, definition of ED, sensitivity and specificity of tests used to diagnose CAD, CVD or PAD, and side-effects of concomitant pharmacological treatment. Moreover, CAD’s clinical characteristics may explain the finding of patients with previous myocardial infarction having normal sexual tests. Indeed, AMI is the initial manifestation of CAD in 30–40% of patients. Since it has been shown that angiographically mild (i.e. <50% diameter stenosis) rather than critical coronary stenoses are those more prone to abruptly occlude and cause infarction [26], patients developing AMI do not necessarily have extensive atherosclerosis when first diagnosed. Consequently, penile circulation, even though affected to a greater extent than coronary circulation, could have not yet reached the critical artery narrowing point so that explains the normal sexual function.

3. Clinical implications

From a practical point of view, clinical significance of ED is different depending on from which side it is viewed. While the detection of ED in a patient with known CAD mainly rises the issue of safety of treatment with oral phosphodiesterase type 5 inhibitors, the detection of isolated ED rises a more important question about concomitant, latent, vascular diseases. Coronary artery disease is by far the most important problem that needs to be investigated. Negative tests are likely to be found in most patients. However, given the high prevalence of common risk factors in this population, a careful medical surveillance is strongly advised.

We urgently need a well-designed longitudinal study evaluating the prevalence and the time of onset of the most common vascular diseases, mainly CAD, in patients with isolated ED. This study should answer the crucial question whether ED can be considered an additional, early sign of vascular disease.

In the meantime, the story of the Titanic disaster, should remind us to keep the eyes wide open against the “tip of the iceberg”.

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